

CLAIMS

This complete listing of the claims, with updated status indicators, is provided below:

Claims 1. - 525. (Canceled)

526. **(Previously Presented)** A reporter signal peptide from about 10 to about 35 amino acids comprising a single amino acid sequence Asp-Pro, wherein the reporter signal peptide can be fragmented across the Asp-Pro peptide bond by collision-induced dissociation in an ion trap mass spectrometer.

527. **(Previously Presented)** The reporter signal peptide of claim 526, further comprising a coupling agent for covalent coupling to a protein or a peptide.

528. **(Previously Presented)** The reporter signal peptide of claim 527, wherein the coupling agent comprises a chemically reactive group.

529. **(Previously Presented)** The reporter signal peptide of claim 528, wherein the coupling agent further comprises a linker linking the chemically reactive group to the reporter signal peptide.

530. **(Previously Presented)** The reporter signal peptide of claim 528, wherein the chemically reactive group can covalently couple with a free sulfhydryl group of a cysteine residue.

531. **(Previously Presented)** The reporter signal peptide of claim 529, wherein the chemically reactive group is selected from the group consisting of thiols, epoxides, or nitriles.

532. **(Previously Presented)** The reporter signal peptide of claim 528, wherein the chemically reactive group can react with a free amino-terminal primary amino group of a protein or a peptide.

533. **(Previously Presented)** The reporter signal peptide of claim 532, wherein the chemically reactive group is selected from the group consisting of an NHS ester and an isothiocyanate.

534. **(Previously Presented)** The reporter signal peptide of claim 533, wherein the chemically reactive group is an NHS ester.

535. **(Previously Presented)** The reporter signal peptide of claim 528, wherein the coupling agent further comprises a linker.
536. **(Previously Presented)** The reporter signal peptide of claim 526 comprising the sequence $(Aa)_n\text{-Asp-Pro-}(Aa)_m$, wherein Aa is an amino acid residue and n and m are each independently an integer of 2 or more and the sum of $n + m$ is about 8 to about 33 amino acids.
537. **(Previously Presented)** The reporter signal peptide of claim 536, wherein the reporter signal peptide sequence is selected from the group consisting of SEQ ID NO:24, SEQ ID NO: 25 and SEQ ID NO: 26.
538. **(Previously Presented)** The reporter signal peptide of claim 526 comprising the sequence $(Aa)_n\text{-Asp-Pro-}(Aa)_m$, wherein n and m is each independently an integer from 2 to 5 and Aa is an amino acid residue.
539. **(Previously Presented)** The reporter signal peptide of claim 538, wherein each amino acid residue Aa is independently selected from the group consisting of glycine, alanine, valine, leucine, and isoleucine.
540. **(Previously Presented)** The reporter signal peptide of claim 539, wherein each amino acid residue Aa is the same amino acid residue.
541. **(Previously Presented)** The reporter signal peptide of claim 540, wherein the amino acid residue Aa is glycine.
542. **(Previously Presented)** The reporter signal peptide of claim 539, wherein m is equal to n.
543. **(Previously Presented)** The reporter signal peptide of claim 526, wherein at least one amino acid is modified by isotopic enrichment, methylation, phosphorylation, sulphation, and use of selenomethionine for methionine.
544. **(Previously Presented)** The reporter signal peptide of claim 543, wherein the at least one modified amino acid is modified by isotopic enrichment.

545. **(Previously Presented)** The reporter signal peptide of claim 544, wherein isotopic enrichment comprises a ^{13}C atom, a ^{15}N atom, a deuterium atom, or any combination thereof.

546. **(Previously Presented)** A set of reporter signal peptides comprising two or more reporter signal peptides of claim 526, wherein each of the reporter signal peptides has the same molecular mass.

547. **(Previously Presented)** The set of reporter signal peptides of claim 546, wherein each of the reporter signal peptides has the same mass-to-charge ratio following ionization in a mass spectrometer.

548. **(Previously Presented)** The set of reporter signal peptides of claim 547, wherein the mass-to-charge ratio of each fragmented reporter signal peptide in the set can be distinguished from the mass-to-charge ratio of the other fragmented reporter signal peptides in the set.

549. **(Previously Presented)** The set of reporter signal peptides of claim 548, wherein the reporter signal peptides further comprise a coupling agent having a chemically reactive group for covalent coupling to a target protein or peptide.

550. **(Previously Presented)** The set of reporter signal peptides of claim 549, wherein the chemically reactive group covalently couples a free sulfhydryl group of the target protein or peptide.

551. **(Previously Presented)** The set of reporter signal peptides of claim 550, wherein the chemically reactive group is selected from the group consisting of: a thiol, an epoxide, and a nitrile.

552. **(Previously Presented)** The set of reporter signal peptides of claim 549, wherein the chemically reactive group covalently couples an amino-terminal primary amine group of the target protein or peptide.

553. **(Previously Presented)** The set of reporter signal peptides of claim 552, wherein the chemically reactive group is selected from the group consisting of: an NHS ester, and an isothiocyanate.

554. **(Previously Presented)** The set of reporter signal peptides of claim 546, wherein the set of reporter signals comprises two or more of CG*G*G*G*DPGGGGR (SEQ ID NO: 1), CG*G*G*GDPGGGG*R (SEQ ID NO: 1), CG*G*GGDPGGG*G*R (SEQ ID NO: 1), CG*GGGDPGG*G*G*R (SEQ ID NO.: 1), and CGGGGDPG*G*G*G*R (SEQ ID NO.: 1), wherein each G* is a glycine with at least one heavy isotope.

555. **(Withdrawn)** A method comprising:

labeling a protein or a peptide in a sample with a reporter signal peptide according to claim 526;

separating the labeled protein or peptide or fragments thereof from molecules having a different mass-to-charge ratio in a mass spectrometer;

fragmenting the reporter signal peptide by collision induced dissociation in an ion trap mass spectrometer; and

detecting fragmented reporter signal peptide.

556. **(Withdrawn)** The method of claim 555, further comprising quantifying the amount of the fragmented reporter signal peptide.

557. **(Withdrawn)** The method of claim 556, further comprising comparing the amount of the fragmented reporter signal peptide to a known or an expected value.

558. **(Withdrawn)** The method of claim 555, further comprising denaturing the protein or peptide prior to labeling it with the reporter signal peptide.

559. **(Withdrawn)** The method of claim 555, further comprising producing the sample by a separation procedure.

560. **(Withdrawn)** The method of claim 559, wherein the separation procedure is selected from the group consisting of liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, and a combination thereof.

561. **(Withdrawn)** The method of claim 555, further comprising fragmenting the labeled protein or peptide before separating the labeled protein or peptide or fragments thereof in a mass spectrometer.

562. **(Withdrawn)** The method of claim 561, wherein the labeled protein or peptide is fragmented by digestion with a protease.

563. **(Withdrawn)** The method of claim 562, wherein the protease is trypsin.

564. **(Withdrawn)** The method of claim 555, wherein the reporter signal peptide comprises one or more of CG*G*G*G*DPGGGGR (SEQ ID NO: 1), CG*G*G*GDPGGGG*R (SEQ ID NO: 1), CG*G*GGDPGGG*G*R (SEQ ID NO: 1), CG*GGGDPGG*G*G*R (SEQ ID NO: 1), CGGGGDPG*G*G*G*R (SEQ ID NO: 1), wherein each G* is a glycine with at least one heavy isotope.

565. **(Withdrawn)** A method comprising:

labeling a set of proteins or peptides in a sample with a set of reporter signal peptides according to claim 546;

separating the set of labeled proteins or peptides or fragments thereof from molecules having a different mass-to-charge ratio in a mass spectrometer;

fragmenting the reporter signal peptides by collision induced dissociation in an ion trap mass spectrometer; and

detecting fragmented reporter signals; and

distinguishing the fragmented reporter signal peptides from each other.

566. **(Withdrawn)** The method of claim 565, further comprising quantifying the amount of a first fragmented reporter signal peptide.

567. **(Withdrawn)** The method of claim 566, further comprising quantifying the amount of a second fragmented reporter signal peptide.

568. **(Withdrawn)** The method of claim 567, further comprising comparing the amounts of the first and the second fragmented reporter signal peptides.

569. **(Withdrawn)** The method of claim 565, wherein the sample is a complex sample comprising multiple proteins.

570. **(Withdrawn)** The method of claim 565, further comprising producing the sample by a separation procedure.

571. **(Withdrawn)** The method of claim 570, wherein the separation procedure is selected from the group consisting of liquid chromatography, gel electrophoresis, two-dimensional chromatography, two-dimensional gel electrophoresis, isoelectric focusing, thin layer chromatography, centrifugation, filtration, ion chromatography, immunoaffinity chromatography, membrane separation, and a combination thereof.

572. **(Withdrawn)** The method of claim 565, further comprising denaturing the set of proteins or peptides prior to labeling them with the set of reporter signals.

573. **(Withdrawn)** The method of claim 565, further comprising fragmenting the labeled proteins or peptides before separating the set of labeled proteins or peptides or fragments thereof in a mass spectrometer.

574. **(Withdrawn)** The method of claim 565, wherein the labeled proteins or peptides are fragmented by digestion with a protease.

575. **(Withdrawn)** The method of claim 565, wherein the protease is trypsin. .

576. **(Withdrawn)** The method of claim 565, wherein the set of reporter signal peptides comprises one of more of CG*G*G*G*DPGGGGR (SEQ ID NO: 1), CG*G*G*GDPGGGG*R (SEQ ID NO: 1), CG*G*GGDPGGG*G*R (SEQ ID NO: 1), CG*GGGDPGG*G*G*R (SEQ ID NO: 1), CGGGGDPG*G*G*G*R (SEQ ID NO: 1), wherein each G* is a glycine with at least one heavy isotope.

577. **(Previously Presented)** A kit comprising:

the set of reporter signal peptides according to claim 546; and

a set of instructions for use.

578. **(Previously Presented)** The kit of claim 577, further comprising at least one target peptide labeled with a reporter signal peptide of claim 526.

579. **(Previously Presented)** The kit of claim 578, wherein the protein or peptide comprises a cysteine amino acid residue.

580. **(Previously Presented)** The kit of claim 577, wherein the set of reporter signals comprises one of more of CG*G*G*G*DPGGGGR (SEQ ID NO: 1), CG*G*G*GDPGGGG*R (SEQ ID NO: 1), CG*G*GGDPGGG*G*R (SEQ ID NO: 1), CG*GGGDPGG*G*G*R (SEQ ID NO: 1), CGGGGDPG*G*G*G*R (SEQ ID NO: 1), wherein each G* is a glycine with at least one heavy isotope.

581. **(Previously Presented)** A protein or peptide labeled with a reporter signal peptide of claim 526.

582. **(Previously Presented)** The protein or peptide of claim 581, wherein the protein or peptide comprises a cysteine amino acid residue.

583. **(Previously Presented)** A set of two or more labeled proteins or peptides according to claim 581.

584. **(Previously Presented)** A set of labeled peptides or proteins labeled with the set of reporter signal peptides of claims 546.

585. **(Previously Presented)** A set of labeled peptides or protein labeled with a set of reporter signals, wherein the set of reporter signals comprises one of more of CG*G*G*G*DPGGGGR (SEQ ID NO: 1), CG*G*G*GDPGGGG*R (SEQ ID NO: 1), CG*G*GGDPGGG*G*R (SEQ ID NO: 1), CG*GGGDPGG*G*G*R (SEQ ID NO: 1), CGGGGDPG*G*G*G*R (SEQ ID NO: 1), wherein each G* is a glycine with at least one heavy isotope.